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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/810,601	03/15/2001	Stephen Donovan	D-2947CIP	9283

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EXAMINER
KAM, CHIH MIN

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 10/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/810,601	DONOVAN, STEPHEN	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cov r sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22 and 24-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22 and 24-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9/16/03* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 22 and 24-30 are pending.

Applicants' amendment filed September 16, 2003 is acknowledged, and applicants' response has been fully considered. Claim 23 has been cancelled, and new claims 24-30 have been added. Therefore, claims 22 and 24-30 are examined.

Objection Withdrawn

2. The previous objection of claim 23 is withdrawn in view of applicants' cancellation of the claim in the amendment filed September 16, 2003.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

3. The previous rejection of claim 23, under 35 U.S.C.112, first paragraph, is withdrawn in view of applicants' cancellation of the claim in the amendment filed September 16, 2003.

4. The previous rejection of claim 23, under 35 U.S.C.112, second paragraph, is withdrawn in view of applicants' cancellation of the claim in the amendment filed September 16, 2003.

Claim Rejections - 35 USC § 103

5. The previous rejection of claims 22 and 23 under 35 U.S.C. 103(a) as being unpatentable over Nett *et al.* (U. S. Patent 5,707,964) in view of Johnson *et al.* (U. S. Patent 5,939,070), is withdrawn in view of applicants' cancellation of the claim, and applicants' response at pages 7-8 of the amendment filed September 16, 2003.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 22 and 24-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a specific gonadotrophin related disease such as prostate cancer, breast cancer or endometrial cancer in a mammal comprising administering an agent of a botulinum toxin (or, a butyricum toxin or a tetani toxin) component, LH_N (the light chain, L and the translocation domain of the heavy chain, H_N) covalently coupled to GnRH or a functional GnRH analog, does not reasonably provide enablement for a method of treating a specific gonadotrophin related disease such as prostate cancer, breast cancer, pancreatic cancer or endometrial cancer in a mammal comprising administering an agent, which comprises a light chain component comprising a light chain of a botulinum toxin, a butyricum toxin or a tetani toxin; a translocation component comprising a heavy chain of a botulinum toxin, a butyricum toxin or a tetani toxin; and a targeting component comprising GnRH or a GnRH analog, where the targeting component selectively binds to a GnRH receptor, wherein the heavy chain contains H_C and H_N. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 22 and 24-30 encompass a method of treating a specific gonadotrophin related disease comprising administering an agent, wherein the agent comprises a light chain component of a botulinum toxin (e.g., type A, B, C1, D, E, F, or G), a butyricum toxin or a tetani toxin; a translocation component of a botulinum toxin, a butyricum toxin or a tetani toxin; and a targeting component of GnRH or GnRH analog which selectively binds to a GnRH receptor. The

specification, however, only discloses cursory conclusions without data supporting the findings, which state that an agent comprising a light chain component of a botulinum toxin, a butyricum toxin or a tetani toxin; a translocation component of a botulinum toxin, a butyricum toxin or a tetani toxin; and a targeting component which selectively binds to a GnRH receptor, can be used for treating a gonadotrophin related disease (pages 22-23). There are no indicia that the present application enables the full scope in view of a method of treating a gonadotrophin related disease using the agent of toxin components and targeting moiety as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses variants regarding the translocation component comprising a heavy chain that contains a translocation domain, H_N and a carboxyl end fragment, H_C involved in binding to cell surface, which are not adequately described or demonstrated in the specification.

(2). The absence of working examples:

There are no working examples indicating the claimed methods in association with the variants except for the agent of LH_N (from BT)-GnRH used for treating prostate cancer,

endometrial cancer and breast cancer (Examples 2, 4 and 5). The specification has not shown the use of an agent such as LH-GnRH, where the heavy chain is intact and contains H_C and H_N, for the treatment of gonadotrophin related cancers.

(3). The state of the prior art and relative skill of those in the art:

The prior art (e.g., Foster et al., WO 96/33273) indicates an agent comprising a clostridial neurotoxin or a hybrid of two clostridial neurotoxins covalently linked to a targeting moiety such as nerve growth factor, where the H_C region of the H-chain has been modified or removed, can be used for alleviating the sensation of pain. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific teachings on the use and the effect of an agent containing the light chain, the heavy chain having H_C and H_N and a GnRH for treating gonadotrophin related cancers to be considered enabling for variants.

(4). The amount of direction or guidance presented and the quantity of experimentation necessary:

Claims 22 and 24-30 are directed to a method of treating a specific gonadotrophin related cancers comprising administering an agent, wherein the agent comprises a light chain component; a translocation component comprising a heavy chain (including H_C and H_N); and a targeting component which selectively binds to a GnRH receptor. The specification indicates an agent comprising a light chain component of a botulinum toxin, a butyricum toxin or a tetani toxin; a translocation component of a botulinum toxin, a butyricum toxin or a tetani toxin; and a targeting component which selectively binds to a GnRH receptor, can be used for treating a gonadotrophin related disease (pages 22-23). However, the specification only demonstrates

using LH_N-GnRH for treating gonadotrophin related cancers (Examples 2, 4 and 5), it does not show the use of the agent containing the light chain, the heavy chain and a GnRH (e.g., LH-GnRH) for treating gonadotrophin related cancers, where the H_C in the heavy chain is not removed or modified. Moreover, the specification has not shown the treating conditions such as the dosage, or the time for the treatment as well as the effects of these agents. There are no working examples indicating the claimed method except for treating gonadotrophin related cancers with LH_N-GnRH. Since the specification fails to provide sufficient teachings on the use and the effect of the agent containing the light chain, the heavy chain and a GnRH for treating gonadotrophin related cancers, it is necessary to have additional guidance and to carry out further experimentation to assess the effect of these agents.

(5). Predictability or unpredictability of the art:

The claims encompass a method of treating gonadotrophin related cancers comprising administering an agent comprising a light chain component, a translocation component comprising a heavy chain, and a targeting component which selectively binds to a GnRH receptor, however, the treating conditions and the effect of these conjugates are not adequately described in the specification, the invention is highly unpredictable regarding the outcome of the treatment.

(6). Nature of the Invention

The scope of the claims encompasses a method of treating gonadotrophin related cancers comprising administering an agent of a light chain component comprising a light chain, a translocation component comprising a heavy chain, and a targeting component of a GnRH which

selectively binds to a GnRH receptor, but the specification does not demonstrate the use and the effect of the agent. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broader than the enabling disclosure, the working examples do not demonstrate the claimed methods associated with variants, the outcome of the treatment is unpredictable, and the teachings in the specification are limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effects of the agents in the treatment of gonadotrophin related cancers.

In response, applicants indicate the claims have been amended to such an enabling claim scope (page 4 of the response). The response has been fully considered, however, the amended claims encompass a method of treatment using an agent of a GnRH and clostridial toxin components having intact H_C, which is not sufficiently described in the specification as indicated in the section above. Therefore, the disclosure is not enabling for the full scope of the claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 22 and 24-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22 and 24-30 are indefinite because the claims lack essential steps in the method of treating a gonadotrophin related illness. The omitted step is the outcome of the treatment. The term "treating a gonadotrophin related illness" is not the end point of the process because it does not address the effect of the agent nor indicates the outcome the treatment. Claims 22 and

24-30 are also indefinite because of the use of the term "GnRH", it is not clear what the term means. A fully spelled out word should be indicated in the first occurrence. Claims 24-28 and 30 are included in the rejection for being dependent on a rejected claim and do not correct the deficiency of the claim from which it depends.

In response, applicants indicate the claims have been amended to address the bases for the rejections (page 5 of the response). The response has been considered, however, the argument is not fully persuasive because the outcome of the treatment has not been indicated in the claims for the reasons shown above.

Conclusions

8. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. C. i K
Patent Examiner

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER

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October 21, 2003